

WHAT IS CLAIMED IS:

1. A method for synthesizing conjugates of one or more synthetic water-soluble polymers with a cytokine, a chemokine, a growth factor or a polypeptide hormone, or an antagonist thereof, that preserves more of the receptor-binding potency of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, than is preserved when such polymers are randomly coupled, comprising:

- (a) selecting a cytokine, chemokine, growth factor or polypeptide hormone in which the amino-terminal amino acid is located remotely from one or more receptor-binding domains of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof; and
- (b) coupling said one or more polymers selectively to said amino-terminal amino acid.

2. The method of claim 1, wherein said one or more polymers is/are selected from the group consisting of one or more polyalkylene glycols, one or more polyalkylene oxides, one or more polyvinyl alcohols, one or more polycarboxylates, one or more poly(vinylpyrrolidones), one or more poly(oxyethylene-oxymethylenes), one or more poly(amino acids), one or more polyacryloylmorpholines, one or more copolymers of one or more amides and one or more alkylene oxides, one or more dextrans and one or more hyaluronic acids.

3. The method of claim 1, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a four helix bundle structure.

4. The method of claim 3, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the

group consisting of macrophage colony-stimulating factor (M-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), leukemia inhibitory factor (LIF), thrombopoietin (Tpo), an erythropoietin (EPO), stem cell factor (SCF), Flt3 ligand, oncostatin M (OSM), an interleukin-2 (IL-2), IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12 (p35 subunit), IL-13, IL-15, IL-17, an interferon-*alpha* (IFN- α), an interferon-*beta* (IFN- β), consensus interferon, prolactin and growth hormone, and muteins, antagonists, variants, analogs and derivatives thereof.

5. The method of claim 1, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a β -sheet or β -barrel structure.

6. The method of claim 5, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of tumor necrosis factor-*alpha* (TNF- α), IL-1 α , IL-1 β , IL-12 (p40 subunit), IL-16, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), acidic FGF, FGF-4 and keratinocyte growth factor (KGF; FGF-7), and muteins, antagonists, variants, analogs and derivatives thereof.

7. The method of claim 1, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a mixed α/β structure.

8. The method of claim 7, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of neutrophil activating peptide-2 (NAP-2), stromal cell-derived factor-1 α (SDF-1 α), IL-8, monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-3, eotaxin-1, eotaxin-2, eotaxin-3, RANTES, myeloid progenitor inhibitory factor-1 (MPIF-1), neurotactin, macrophage migration inhibitory factor (MIF) and growth-related oncogene/melanoma growth

stimulatory activity (GRO- α /MGSA), and muteins, antagonists, variants, analogs and derivatives thereof.

9. The method of claim 1, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of an interferon-*alpha*, an interferon-*beta*, an IL-2, IL-4, IL-10, TNF-*alpha*, IGF-1, EGF, bFGF, insulin, a TNF-*alpha* antagonist, an hGH antagonist and a prolactin antagonist.

10. The method of claim 9, wherein said cytokine is an IL-2.

11. The method of claim 9, wherein said cytokine is an interferon-*alpha*.

12. The method of claim 9, wherein said cytokine is TNF-*alpha*.

13. The method of claim 9, wherein said cytokine antagonist is a TNF-*alpha* antagonist.

14. The method of claim 9, wherein said growth factor is EGF.

15. The method of claim 9, wherein said growth factor is IGF-1.

16. The method of claim 1, wherein said polymer is covalently coupled to the *alpha* amino group of said amino-terminal amino acid.

17. The method of claim 16, wherein said covalent coupling of said polymer to said *alpha* amino group is *via* a secondary amine linkage.

18. The method of claim 1, wherein said polymer is coupled to a chemically reactive side chain group of said amino-terminal amino acid.

19. The method of claim 18, wherein said reactive side chain is selected from the group consisting of a hydroxyl group, a sulfhydryl group, a

guanidino group, an imidazole group, an amino group, a carboxyl group and an aldehyde group.

20. The method of claim 1, wherein said water-soluble polymer is a polyalkylene glycol.

21. The method of claim 20, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol), a monomethoxypoly(ethylene glycol) and a monohydroxypoly(ethylene glycol).

22. The method of claim 21, wherein said polyalkylene glycol is a monomethoxypoly(ethylene glycol).

23. The method of claim 21, wherein said polyalkylene glycol is a monohydroxypoly(ethylene glycol).

24. The method of claim 20, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 100 kDa, inclusive.

25. The method of claim 24, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 5 kDa, inclusive.

26. The method of claim 24, wherein said polyalkylene glycol has a molecular weight of between about 10 kDa and about 20 kDa, inclusive.

27. The method of claim 24, wherein said polyalkylene glycol has a molecular weight of between about 18 kDa and about 60 kDa, inclusive.

28. The method of claim 24, wherein said polyalkylene glycol has a molecular weight of between about 12 kDa and about 30 kDa, inclusive.

29. The method of claim 28, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

30. The method of claim 24, wherein said polyalkylene glycol has a molecular weight of about 30 kDa.

31. The method of claim 4, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of prolactin and prolactin analogs that mimic or antagonize the biological effects of prolactin that are mediated by prolactin receptors.

32. The method of claim 4, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of growth hormone and growth hormone analogs that mimic or antagonize the biological effects of growth hormone that are mediated by growth hormone receptors.

33. The method of claim 4, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of nonglycosylated erythropoietin and erythropoietin analogs that mimic or antagonize the biological effects of erythropoietin that are mediated by erythropoietin receptors.

34. The method of claim 1, wherein the coupling of said polymer to said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, at said amino-terminal amino acid mimics the beneficial effects of glycosylation or hyperglycosylation of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof.

35. The method of claim 1, wherein said receptor-binding potency is measured by one or more methods selected from the group including ultracentrifugation, cell-based assays, competitive binding assays, radioreceptor assays, surface plasmon resonance and dynamic light scattering.

36. A conjugate produced by the method of claim 1.

37. A pharmaceutical composition comprising one or more of the conjugates of claim 36 and one or more pharmaceutically acceptable excipients or carriers.

38. A conjugate comprising a cytokine, a chemokine, a growth factor or a polypeptide hormone, or antagonist thereof, coupled to one or more synthetic water-soluble polymers, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected for its membership in the group of receptor-binding proteins and polypeptides in which the amino-terminal amino acid is located remotely from one or more receptor-binding domains and wherein said one or more polymers is/are coupled to said amino-terminal amino acid.

39. The conjugate of claim 38, wherein said one or more polymers is/are selected from the group consisting of one or more polyalkylene glycols, one or more polyalkylene oxides, one or more polyvinyl alcohols, one or more polycarboxylates, one or more poly(vinylpyrrolidones), one or more poly(oxyethylene-oxyethylenes), one or more poly(amino acids), one or more polyacryloylmorpholines, one or more copolymers of one or more amides and one or more alkylene oxides, one or more dextrans and one or more hyaluronic acids.

40. The conjugate of claim 38, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a four helix bundle structure.

41. The conjugate of claim 40, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of macrophage colony-stimulating factor (M-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), leukemia inhibitory factor (LIF), thrombopoietin (Tpo), an erythropoietin (EPO), stem cell factor (SCF), Flt3 ligand, oncostatin M (OSM), an interleukin-2 (IL-2), IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12 (p35 subunit), IL-13,

IL-15, IL-17, an interferon *alpha* (IFN- α), an interferon *beta* (IFN- β), consensus interferon, prolactin and growth hormone, and muteins, antagonists, variants, analogs and derivatives thereof.

42. The conjugate of claim 38, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a β -sheet or β -barrel structure.

43. The conjugate of claim 42, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of tumor necrosis factor *alpha* (TNF- α), IL-1 α , IL-1 β , IL-12 (p40 subunit), IL-16, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), acidic FGF, FGF-4 and keratinocyte growth factor (KGF; FGF-7), and muteins, antagonists, variants, analogs and derivatives thereof.

44. The conjugate of claim 38, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a mixed α/β structure.

45. The conjugate of claim 44, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of neutrophil activating peptide-2 (NAP-2), stromal cell-derived factor-1 α (SDF-1 α), IL-8, monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-3, eotaxin-1, eotaxin-2, eotaxin-3, RANTES, myeloid progenitor inhibitory factor-1 (MPIF-1), neurotactin, macrophage migration inhibitory factor (MIF) and GRO/melanoma growth stimulatory activity (GRO- α /MGSA), and muteins, variants, analogs and derivatives thereof.

46. The conjugate of claim 38, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of an interferon-*alpha*, an interferon-*beta*, an IL-2, IL-4,

IL-10, TNF-*alpha*, IGF-1, EGF, bFGF, hGH, insulin and prolactin, and antagonists thereof.

47. The conjugate of claim 46, wherein said cytokine is an IL-2.

48. The conjugate of claim 46, wherein said cytokine is an interferon-*alpha*.

49. The conjugate of claim 46, wherein said cytokine is TNF-*alpha*.

50. The conjugate of claim 46, wherein said cytokine antagonist is a TNF-*alpha* antagonist.

51. The conjugate of claim 46, wherein said growth factor is EGF.

52. The conjugate of claim 46, wherein said growth factor is IGF-1.

53. The conjugate of claim 38, wherein said polymer is covalently coupled to the *alpha* amino group of said amino-terminal amino acid.

54. The conjugate of claim 53, wherein said covalent coupling of said polymer to said *alpha* amino group is *via* a secondary amine linkage.

55. The conjugate of claim 38, wherein said polymer is coupled to a chemically reactive side chain group of said amino-terminal amino acid.

56. The conjugate of claim 55, wherein said reactive side chain is selected from the group consisting of a hydroxyl group, a sulfhydryl group, a guanidino group, an imidazole group, an amino group, a carboxyl group and an aldehyde group.

57. The conjugate of claim 38, wherein said water-soluble polymer is a polyalkylene glycol.

58. The conjugate of claim 57, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol), a monomethoxypoly(ethylene glycol) and a monohydroxypoly(ethylene glycol).

59. The conjugate of claim 58, wherein said polyalkylene glycol is a monomethoxypoly(ethylene glycol).

60. The conjugate of claim 58, wherein said polyalkylene glycol is a monohydroxypoly(ethylene glycol).

61. The conjugate of claim 57, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 100 kDa, inclusive.

62. The conjugate of claim 61, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 5 kDa, inclusive.

63. The conjugate of claim 61, wherein said polyalkylene glycol has a molecular weight of between about 10 kDa and about 20 kDa, inclusive.

64. The conjugate of claim 61, wherein said polyalkylene glycol has a molecular weight of between about 18 kDa and about 60 kDa, inclusive.

65. The conjugate of claim 61, wherein said polyalkylene glycol has a molecular weight of between about 12 kDa and about 30 kDa, inclusive.

66. The conjugate of claim 65, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

67. The conjugate of claim 61, wherein said polyalkylene glycol has a molecular weight of about 30 kDa.

68. The conjugate of claim 40, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of prolactin and prolactin analogs that mimic or antagonize the biological effects of prolactin that are mediated by prolactin receptors.

69. The conjugate of claim 40, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of growth hormone and growth hormone analogs that mimic or antagonize the biological effects of growth hormone that are mediated by growth hormone receptors.

70. The conjugate of claim 41, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of nonglycosylated erythropoietin and erythropoietin analogs that mimic or antagonize the biological effects of erythropoietin that are mediated by erythropoietin receptors.

71. The conjugate of claim 38, wherein the coupling of said polymer to said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, at said amino-terminal amino acid mimics the beneficial effects of glycosylation or hyperglycosylation of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof.

72. A pharmaceutical composition comprising the conjugate of claim 38 and a pharmaceutically acceptable carrier or excipient.

73. A kit comprising the pharmaceutical composition of claim 37.

74. A kit comprising the conjugate of claim 38.

75. A kit comprising the conjugate of claim 40.

76. A kit comprising the pharmaceutical composition of claim 72.

77. A method for synthesizing conjugates of one or more synthetic water-soluble polymers with a cytokine, a chemokine, a growth factor or a polypeptide hormone, or antagonist thereof, that preserves more of the receptor-binding potency of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, than is preserved when such polymers are randomly coupled, comprising:

- (a) selecting a cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, in which a naturally occurring or genetically engineered glycosylation site is located remotely from one or more receptor-binding domains of said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof; and
- (b) coupling said one or more polymers selectively to said glycosylation site or to a carbohydrate moiety attached thereto.

78. The method of claim 77, wherein said one or more polymers is/are selected from the group consisting of one or more polyalkylene glycols, one or more polyalkylene oxides, one or more polyvinyl alcohols, one or more polycarboxylates, one or more poly(vinylpyrrolidones), one or more poly(oxyethylene-oxymethylene), one or more poly(amino acids) one or more polyacryloylmorpholines, one or more copolymers of one or more amides and one or more alkylene oxides, one or more dextrans and one or more hyaluronic acids.

79. The method of claim 77, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a four helix bundle structure.

80. The method of claim 79, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of macrophage colony-stimulating factor (M-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), leukemia inhibitory factor (LIF), thrombopoietin (Tpo), an erythropoietin (EPO), stem cell factor (SCF), Flt3 ligand, oncostatin M (OSM), an interleukin-2 (IL-2), IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12 (p35 subunit), IL-13, IL-15, IL-17, an interferon *alpha* (IFN- α), an interferon *beta* (IFN- β),

consensus interferon, prolactin and growth hormone, and muteins, antagonists, variants, analogs and derivatives thereof.

81. The method of claim 77, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a β -sheet or β -barrel structure.

82. The method of claim 81, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of tumor necrosis factor *alpha* (TNF- α), IL-1 α , IL-1 β , IL-12 (p40 subunit), IL-16, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), acidic FGF, FGF-4 and keratinocyte growth factor (KGF; FGF-7), and muteins, antagonists, variants, analogs and derivatives thereof.

83. The method of claim 77, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a mixed α/β structure.

84. The method of claim 83, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of neutrophil activating peptide-2 (NAP-2), stromal cell-derived factor-1 α (SDF-1 α), IL-8, monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-3, eotaxin-1, eotaxin-2, eotaxin-3, RANTES, myeloid progenitor inhibitory factor-1 (MPIF-1), neurotactin, macrophage migration inhibitory factor (MIF) and GRO/melanoma growth stimulatory activity (GRO- α /MGSA), and muteins, variants, analogs and derivatives thereof.

85. The method of claim 77, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of an interferon-*alpha*, an interferon-*beta*, an IL-2, IL-4, IL-10, TNF-*alpha*, IGF-1, EGF, bFGF, hGH, prolactin, insulin, and antagonists thereof.

86. The method of claim 85, wherein said cytokine is an IL-2.

87. The method of claim 85, wherein said cytokine is an interferon-*alpha*.

88. The method of claim 85, wherein said cytokine is TNF-*alpha*.

89. The method of claim 85, wherein said cytokine antagonist is a TNF-*alpha* antagonist.

90. The method of claim 85, wherein said growth factor is EGF.

91. The method of claim 85, wherein said growth factor is IGF-1.

92. The method of claim 77, wherein said water-soluble polymer is a polyalkylene glycol.

93. The method of claim 92, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol), a monomethoxypoly(ethylene glycol) and a monohydroxypoly(ethylene glycol).

94. The method of claim 93, wherein said polyalkylene glycol is a monomethoxypoly(ethylene glycol).

95. The method of claim 93, wherein said polyalkylene glycol is a monohydroxypoly(ethylene glycol).

96. The method of claim 92, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 100 kDa, inclusive.

97. The method of claim 96, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 5 kDa, inclusive.

98. The method of claim 96, wherein said polyalkylene glycol has a molecular weight of between about 10 kDa and about 20 kDa, inclusive.

99. The method of claim 96, wherein said polyalkylene glycol has a molecular weight of between about 18 kDa and about 60 kDa, inclusive.

100. The method of claim 96, wherein said polyalkylene glycol has a molecular weight of between about 12 kDa and about 30 kDa, inclusive.

101. The method of claim 100, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

102. The method of claim 96, wherein said polyalkylene glycol has a molecular weight of about 30 kDa.

103. The method of claim 77, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of prolactin and prolactin analogs that mimic or antagonize the biological effects of prolactin that are mediated by prolactin receptors.

104. The method of claim 77, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of growth hormone and growth hormone analogs that mimic or antagonize the biological effects of growth hormone that are mediated by growth hormone receptors.

105. The method of claim 77, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of nonglycosylated erythropoietin and erythropoietin analogs that mimic or antagonize the biological effects of erythropoietin that are mediated by erythropoietin receptors.

106. The method of claim 77, wherein the coupling of said polymer to said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, at or near said glycosylation site or sites mimics the beneficial effects of glycosylation or hyperglycosylation of said cytokine, chemokine, growth factor or polypeptide hormone.

107. A conjugate produced by the method of claim 77.

108. A pharmaceutical composition comprising one or more of the conjugates of claim 107 and one or more pharmaceutically acceptable excipients or carriers.

109. A conjugate comprising a cytokine, a growth factor, a chemokine or a polypeptide hormone, or antagonist thereof, coupled to one or more synthetic water-soluble polymers, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected for its membership in the group of receptor-binding proteins and polypeptides in which a glycosylation site is located remotely from one or more receptor-binding domains and wherein said one or more polymers is/are coupled at or near one or more glycosylation sites or to a carbohydrate moiety attached thereto.

110. The conjugate of claim 109, wherein said one or more polymers is/are selected from the group consisting of one or more polyalkylene glycols, one or more polyalkylene oxides, one or more polyvinyl alcohols, one or more polycarboxylates, one or more poly(vinylpyrrolidones), one or more poly(oxyethylene-oxyethylenes), one or more poly(amino acids), one or more polyacryloylmorpholines, one or more copolymers of one or more amides and one or more alkylene oxides, one or more dextrans and one or more hyaluronic acids.

111. The conjugate of claim 109, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a four helix bundle structure.

112. The conjugate of claim 111, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of macrophage colony-stimulating factor (M-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), leukemia

inhibitory factor (LIF), thrombopoietin (Tpo), an erythropoietin (EPO), stem cell factor (SCF), Flt3 ligand, oncostatin M (OSM), an interleukin-2 (IL-2), IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12 (p35 subunit), IL-13, IL-15, IL-17, an interferon *alpha* (IFN- α), an interferon *beta* (IFN- β), consensus interferon, prolactin and growth hormone, and muteins, antagonists, variants, analogs and derivatives thereof.

113. The conjugate of claim 109, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a β -sheet or β -barrel structure.

114. The conjugate of claim 113, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of tumor necrosis factor *alpha* (TNF- α), IL-1 α , IL-1 β , IL-12 (p40 subunit), IL-16, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), acidic FGF, FGF-4 and keratinocyte growth factor (KGF; FGF-7), and muteins, antagonists, variants, analogs and derivatives thereof.

115. The conjugate of claim 109, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, has a mixed α/β structure.

116. The conjugate of claim 115, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of neutrophil activating peptide-2 (NAP-2), stromal cell-derived factor-1 α (SDF-1 α), IL-8, monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-3, eotaxin-1, eotaxin-2, eotaxin-3, RANTES, myeloid progenitor inhibitory factor-1 (MPIF-1), neurotactin, macrophage migration inhibitory factor (MIF) and growth-related oncogene/melanoma growth stimulatory activity (GRO- α /MGSA), and muteins, antagonists, variants, analogs and derivatives thereof.

117. The conjugate of claim 109, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of an interferon-*alpha*, an interferon-*beta*, an IL-2, IL-4, IL-10, TNF-*alpha*, IGF-1, EGF, bFGF, hGH, prolactin, insulin, and antagonists thereof.

118. The conjugate of claim 117, wherein said cytokine is an IL-2.

119. The conjugate of claim 117, wherein said cytokine is an interferon-*alpha*.

120. The conjugate of claim 117, wherein said cytokine is TNF-*alpha*.

121. The conjugate of claim 117, wherein said cytokine antagonist is a TNF-*alpha* antagonist.

122. The conjugate of claim 117, wherein said growth factor is EGF.

123. The conjugate of claim 117, wherein said growth factor is IGF-1.

124. The conjugate of claim 109, wherein said water-soluble polymer is a polyalkylene glycol.

125. The conjugate of claim 124, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol), a monomethoxypoly(ethylene glycol) and a monohydroxypoly(ethylene glycol).

126. The conjugate of claim 125, wherein said polyalkylene glycol is a monomethoxypoly(ethylene glycol).

127. The conjugate of claim 125, wherein said polyalkylene glycol is a monohydroxypoly(ethylene glycol).

128. The conjugate of claim 124, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 100 kDa, inclusive.

129. The conjugate of claim 128, wherein said polyalkylene glycol has a molecular weight of between about 1 kDa and about 5 kDa, inclusive.

130. The conjugate of claim 128, wherein said polyalkylene glycol has a molecular weight of between about 10 kDa and about 20 kDa, inclusive.

131. The conjugate of claim 128, wherein said polyalkylene glycol has a molecular weight of between about 18 kDa and about 60 kDa, inclusive.

132. The conjugate of claim 128, wherein said polyalkylene glycol has a molecular weight of between about 12 kDa and about 30 kDa, inclusive.

133. The conjugate of claim 132, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

134. The conjugate of claim 128, wherein said polyalkylene glycol has a molecular weight of about 30 kDa.

135. The conjugate of claim 109, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of prolactin and prolactin analogs that mimic or antagonize the biological effects of prolactin that are mediated by prolactin receptors.

136. The conjugate of claim 109, wherein said polypeptide hormone, or antagonist thereof, is selected from the group consisting of growth hormone and growth hormone analogs that mimic or antagonize the biological effects of growth hormone that are mediated by growth hormone receptors.

137. The conjugate of claim 109, wherein said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, is selected from the group consisting of nonglycosylated erythropoietin and erythropoietin analogs that mimic or antagonize the biological effects of erythropoietin that are mediated by erythropoietin receptors.

138. The conjugate of claim 109, wherein the coupling of said polymer to said cytokine, chemokine, growth factor or polypeptide hormone, or antagonist thereof, at or near said glycosylation site mimics the beneficial effects of glycosylation or hyperglycosylation of said cytokine, chemokine, growth factor or polypeptide hormone.

139. A pharmaceutical composition comprising the conjugate of claim 109 and a pharmaceutically acceptable carrier or excipient.

140. A kit comprising the conjugate of claim 107.

141. A kit comprising the pharmaceutical composition of claim 108.

142. A kit comprising the conjugate of claim 109.

143. A kit comprising the pharmaceutical composition of claim 139.

144. A method for preventing, diagnosing, or treating a physical disorder in an animal suffering from or predisposed to said physical disorder, comprising administering to said animal an effective amount of the conjugate of any one of claims 36, 38, 107 and 109.

145. A method for preventing, diagnosing, or treating a physical disorder in an animal suffering from or predisposed to said physical disorder, comprising administering to said animal an effective amount of the pharmaceutical composition of any one of claims 37, 72, 108 and 139.

146. The method of claim 144, wherein said animal is a mammal.

147. The method of claim 145, wherein said animal is a mammal.

148. The method of claim 146 or claim 147, wherein said mammal is a human.

149. The method of claim 144, wherein said physical disorder is selected from the group consisting of a cancer, an infectious disease, a neurodegenerative disorder, an autoimmune disorder, and a genetic disorder.

150. The method of claim 149, wherein said cancer is selected from the group consisting of a breast cancer, a uterine cancer, an ovarian cancer, a prostate cancer, a testicular cancer, a lung cancer, a leukemia, a lymphoma, a colon cancer, a gastrointestinal cancer, a pancreatic cancer, a bladder cancer, a kidney cancer, a bone cancer, a neurological cancer, a head and neck cancer, a skin cancer, a sarcoma, a carcinoma, an adenoma and a myeloma.

151. The method of claim 149, wherein said infectious disease is selected from the group consisting of a bacterial disease, a fungal disease, a viral disease and a parasitic disease.

152. The method of claim 151, wherein said viral disease is selected from the group consisting of hepatitis B, hepatitis C, a disease caused by a cardiotropic virus and HIV/AIDS.

153. The method of claim 149, wherein said autoimmune disorder is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis and psoriasis.

154. The method of claim 149, wherein said genetic disorder is selected from the group consisting of anemia, neutropenia, thrombocytopenia, hemophilia, dwarfism and severe combined immunodeficiency disease ("SCID").

155. The method of claim 149, wherein said neurodegenerative disorder is multiple sclerosis.

156. The method of claim 149, wherein said neurodegenerative disease is Creutzfeldt-Jakob disease or Alzheimer's disease.

157. The method of claim 145, wherein said physical disorder is selected from the group consisting of a cancer, an infectious disease, a neurodegenerative disorder, an autoimmune disorder, and a genetic disorder.

158. The method of claim 157, wherein said cancer is selected from the group consisting of a breast cancer, a uterine cancer, an ovarian cancer, a prostate cancer, a testicular cancer, a lung cancer, a leukemia, a lymphoma, a colon cancer, a gastrointestinal cancer, a pancreatic cancer, a bladder cancer, a kidney cancer, a bone cancer, a neurological cancer, a head and neck cancer, a skin cancer, a sarcoma, a carcinoma, an adenoma and a myeloma.

159. The method of claim 157, wherein said infectious disease is selected from the group consisting of a bacterial disease, a fungal disease, a viral disease and a parasitic disease.

160. The method of claim 159, wherein said viral disease is selected from the group consisting of hepatitis B, hepatitis C, a disease caused by a cardiotropic virus and HIV/AIDS.

161. The method of claim 157, wherein said autoimmune disorder is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis and psoriasis.

162. The method of claim 157, wherein said genetic disorder is selected from the group consisting of anemia, neutropenia, thrombocytopenia, hemophilia, dwarfism and severe combined immunodeficiency disease ("SCID").

163. The method of claim 157, wherein said neurodegenerative disorder is multiple sclerosis.

164. The method of claim 157, wherein said neurodegenerative disease is Creutzfeldt-Jakob disease or Alzheimer's disease.